WS6.5 Body mass index, carbohydrate intake and insulin dosage per carbohydrate unit in 131 female and 77 male patients with cystic fibrosis-related diabetes

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Objectives: Secondary diabetes becomes more prevalent in CF. However, research on CF-related diabetes (CFRD) is still rare. We analyzed BMI, carbohydrate intake and insulin requirement per carbohydrate unit (1 CU equals 11g carbohydrates) in CFRD.
Methods: Until March 2013, the multicenter, prospective German/Austrian diabetes patient registry (DPV) comprised anonymized data on 208 insulin-treated CFRD patients (63% female) with age >5 years at diabetes onset and without tube feeding, lung transplantation or systemic steroid therapy. Median age (IQR) was 18.3 (5.7) years for females and 18.9 (4.3) years for males. Gender-specific analyses were carried out. To compare hemoglobin A1c (HbA1c), carbohydrate intake and insulin requirement per CU, hierarchic multivariable regression models were applied. All analyses were done with SAS 9.4.
Results: 80.0% of females and 80.3% of males did not achieve gender- and age-specific ADA recommendations for BMI (Moran et al., 2010). Based on WHO criteria, 34.6% of females and 39.5% of males had a BMI <18.5 kg/m^2. Using the 10th BMI-percentile, 32.3% of females and 39.5% of males were underweight. After adjustment for age, males had a higher carbohydrate intake than females (254±11 vs. 219±9g, p = 0.012). Metabolic control assessed by HbA1c (females vs. males: 7.6±0.2 vs. 7.9±0.2%) and insulin requirement per CU (1.33±0.09 vs. 1.23±0.11 IU/CU*d) did not differ significantly between genders.
Conclusion: About one third of insulin-treated CFRD patients revealed a poor nutritional status. Despite a higher carbohydrate intake in males, no gender difference was observed for insulin requirement per carbohydrate unit.

WS6.6 Continuous glucose monitoring is a useful tool for diagnosis of cystic fibrosis related diabetes

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Objectives: The diagnosis of CF related diabetes (CFRD) is traditionally by WHO criteria with acknowledgement that they are not ideal for CF. Continuous glucose monitoring (CGM) is used as a diagnostic tool in this unit as well as OGTT. CGM gives a measure of % time above the upper limit of normal for glucose (7.8 mmol/L), as well as capturing peaks of glucose over the DM diagnostic cut off of 11.1.
Aims: To compare glycaemic and clinical parameters of children whose CGM resulted in starting insulin therapy to those whose did not. All were screened for CFRD on clinical suspicion (poor wt, unexplained deterioration, high random glucose) or raised HbA1c.
Methods: A retrospective audit of CGM data (iPro2) obtained on CF children 2010–13 at the Royal Brompton Hospital, London.
Results: 44 children screened with CGM (18 male), median age 13.8 yrs (IQ range 12.1–15.2). The median length of recording was 4 days. 15 children were started on insulin based on CGM results, median age 13 yrs of those who commenced insulin therapy vs 14 yrs who did not, FEV_1 z-score −2.29 vs −1.52, BMI z-score −0.04 vs −0.8. Percentage time >7.8 was 26% vs 5% ($p < 0.001$) and time within 3.9–7.8 was 68% vs 89% ($p < 0.001$). There was no correlation between glucose % time >7.8 and HbA1c although there was a slightly higher proportion with raised HbA1c in the diagnostic group 8/15 (53%) vs 8/29 (28%) and no significant difference in HbA1c between the two groups 6.3% vs 5.9%.
Conclusion: The combination of CGM results and clinical status is invaluable in the decision-making process regarding starting insulin within the paediatric CF population.

WS6.7 Cystic fibrosis and bone disease: defective osteoblast maturation with the F508del mutation in CFTR

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Low bone density is commonly seen in patients with cystic fibrosis (CF) and begins at a young age. The underlying molecular defect in CFTR caused by the F508del-CFTR mutation in osteoblastogenesis, i.e., on the bone formation is unknown. We investigated whether the F508del mutation could affect the expression of osteoblast genes relative to differentiation [collagen type 1, osteocalcin (OC), osteopontin (ON), alkaline phosphatase (ALPL), RUNX2, OSX] and maturation [BMP2, SMAD1/2, osteoprotegerin (OPG), receptor activator of NF-κB ligand (RANKL), cyclooxygenase-2 (COX-2)] in osteoblasts. CF osteoblasts were obtained from bone explants prepared from rib fragments harvested during lung transplantation in four young patients with the F508del mutation in CFTR. We showed evidence of CFTR-dependent chloride activity in normal osteoblasts, which was reduced in CF osteoblasts. Compared to normal osteoblasts, real time PCR data showed no difference in differentiation genes in CF osteoblasts. But, a severe defective maturation of CF osteoblasts was found in four CF patients. CF osteoblasts exhibited a lower expression of SMAD2, COX-2, but a higher RANKL/OPG ratio. Production of COX-2 metabolite prostaglandin E2 (PGE2) was reduced by CF osteoblasts. Treatment with the CFTR correctors (a potentiator VRT-532, a correctorVRT-534) increased the F508del-CFTR channel activity, ameliorated both the RANKL/OPG mRNA ratio and COX-2/PGE2 expression and production. The effect of such drugs on the maturation-related genes of F508del osteoblast and their effects on bone mass and formation needs to be investigated for treatment of CF bone disease.
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WS6.8 Acute kidney injury afflicts a significant proportion of adult patients with cystic fibrosis, with an incidence in excess of that of the general population which clusters with specific risk factors

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Objectives: As patients with cystic fibrosis (PWCF) age, we witness an increase in other comorbid conditions. Amongst these is acute kidney injury (AKI). We studied the incidence of AKI in an adult cohort of PWCF.
Methods: Retrospective single-centre observational cohort study of 120 adult PWCF (aged 18–50 yrs) for the period 01/01/11–31/12/12. Patient records were interrogated to detect evidence of AKI, as defined by the KDIGO 2012 Clinical Practice Guideline for Acute Kidney Injury.
Results: 74 (62%) male. Median (IQR) age 27 (21, 31) yrs. At 01/01/11, 13 (11%) had chronic kidney disease (CKD); none subsequently developed this. 25 (21%) had cystic fibrosis-related diabetes (CFRD); 5 (4%) subsequently developed this. 10 (8%) had received an organ transplant before 01/11/11; 4 (3%) received a transplant during the study period. 5 (4%) male patients died.
20 (17%) patients (11 male) experienced 57 individual episodes of AKI. This annual incidence of ~250,000 cases pmp is >200 times that reported for the general population. Mean AKI episodes per affected patient was 3, the majority being graded AKIN Stage 1.
Of the 20 patients experiencing AKI, 6 (30%) had pre-existing CKD; 8 (40%) had pre-existing CFRD; 7 (35%) had an organ transplant. 48/120 (40%) of patients had at least one of these three co-morbidities. Although not all of these experienced an episode of AKI, 75% of all AKI episodes occurred within this sub-group.
Conclusion: AKI incidence is very common in this cohort. A subgroup defined by 3 risk factors had a 1-in-3 probability of developing AKI over a 2 year period. Focussing preventative strategies and researching risk in this group would seem appropriate.